AF

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/607,565	06/27/2003	Steven M. Ruben	PZ033P1C2	5160

22195 7590 09/27/2005

HUMAN GENOME SCIENCES INC
INTELLECTUAL PROPERTY DEPT.
14200 SHADY GROVE ROAD
ROCKVILLE, MD 20850

EXAMINER	
LEE, BETTY L	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 09/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/607,565	RUBEN ET AL.	
	Examiner	Art Unit	
	Betty Lee, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-48* is/are pending in the application.

4a) Of the above claim(s) *1-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed July 6, 2005 is acknowledged. Applicant's election of Group 44 (polypeptides of SEQ ID NO: 60 and 83, encoded by cDNA Clone ID HCNDA61) is noted. Claims 1-24 are canceled. New claims 25-48 are added. Claims 25-48 are pending and under examination.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Human Secreted Protein Expressed in Colon Cells.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "written description" rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description"

Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the "written description" inquiry, is *whatever is now claimed*" (see page 1117). A review of the language of the claim indicates that these claims are drawn to a genus, i.e., polypeptides that comprise SEQ ID NO: 60 or 83, polypeptides that comprise fragments of SEQ ID NO: 60 or 83 with 30 or 50 contiguous amino acids, and variants of SEQ ID NO: 60 or 83 with 95% or greater sequence identity.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states "An adequate written description of a DNA ... requires a precise definition, such as by

structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention".

There are 4 species of the claimed genus disclosed that are within the scope of the claimed genus, *i.e.* polypeptides consisting of the amino acid sequence of the full length SEQ ID NO: 60 or 83, polypeptides of aa 24-327 of SEQ ID NO: 60,polypeptides of aa 24-245 of SEQ ID NO: 83. The disclosure of even a single species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claims encompass numerous species that are not further described. There is substantial variability among the species.

One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus of proteins which comprise variants 95% or greater sequence identity with SEQ ID NO: 60 or 83 and fragments of SEQ ID NO: 60 or 83. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (see *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structures of the proteins encompassed within the claimed genus of proteins.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 25 and 37 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a product found in nature. Products of nature e.g. polypeptides, do not constitute patentable subject matter. See MPEP 2105. The polypeptides are products of nature as evidenced by Lal, *et al* (WO0000610) and Baker, *et al* (US20030027988) Lal, *et al* teach that human signal peptide-containing protein HSPP-28 shows 99.7% homology with the polypeptide of SEQ ID NO: 60 from 1-327 aa and Baker, *et al* teach that Sequence 236 shows 100% homology with the polypeptide of SEQ ID NO: 83 from 1-243 aa. Examiner suggests the use of the term 'isolated' before polypeptide.

Claims 25-48 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The claims are drawn to a polypeptide of SEQ ID NO: 60 or 83, which is encoded by a gene which is believed to reside on chromosome 11 and is expressed primarily in colon tissue. The specification asserts the following utilities for the polypeptide, all of which are credible, but none of which are specific and substantial:

a) Polynucleotides encoding and polypeptides of SEQ ID NO: 60 or 83 are of interest in relation to methods of treatment of certain diseases (pp. 38- 39), and could be used for the diagnosis or treatment of diseases including tumors, of the intestine, cancer of the colon and rectum (pp. 39, paragraph 0105). The specification asserts that "polynucleotides and polypeptides of the invention are useful for differential identification

of the tissue(s) or cell type(s) present in biological sample and for diagnosis of diseases and conditions which include, but are not limited to, proliferative disorders, particularly of the immune or gastrointintestinal system, such as colon cancer". This utility is neither specific nor substantial. In order for the utility to be specific, applicant would have to demonstrate a nexus between the claimed invention (i.e. polypeptides of SEQ ID NO: 60 or 83) and a specific disease, condition, or disorder. Applicant has not done this, but has merely stated that the polypeptides of the present invention are useful for diagnosis of proliferative disorders, which amounts to a non-limiting list of diseases which may be of interest. Simply stating that the polypeptides of the instant invention may be used to diagnose a proliferative disorder does not mean that the polypeptide or polynucleotide has any physiological relevance to any particular proliferative disease. Furthermore, this utility is not substantial. In order for a utility to be substantial, it must be clear from the specification that the invention is ready to use in current form, i.e. without further research being necessary. In the instant case, a significant amount of further research would be necessary to use the polynucleotides and polypeptides as asserted. Applicant has stated that " the protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy". (pg 39, paragraph 0105), but has not stated what those functions are, or even defined how they are relevant. There is no demonstration of whether expression levels of the instant polypeptides are modulated, either up or down, in any of the diseases. It is not possible to use the invention to diagnose any disease, since applicant has not shown a statistically significant change in the expression or activity of the polypeptides that is correlated with any disease or

condition. It is not possible to use the polypeptides of SEQ ID NO: 60 or 83 to treat any condition, since applicant has not shown that the instant polynucleotides or polypeptides are useful in doing so in any experimental system or in human patients. As stated in MPEP § 2107.01, assertions that a novel DNA is useful for

> "diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed. Contrast the situation where an applicant *discloses a specific biological activity and reasonably correlates that activity to a disease condition* [emphasis added]. Assertions falling within the latter category generally are sufficient to identify a specific utility for the invention. Assertions that fall in the former category are insufficient to define a specific utility for the inventions, especially if the assertion takes the form of a general statement that makes it clear that a "useful" invention may arise from what has been disclosed by the applicant. *Knapp v. Anderson*, 477 F.2d 588, 177 USPQ 688 (CCPA 1973)."

Although the example given by the MPEP above is drawn to an asserted utility for a DNA as a diagnostic marker, the same logic can be applied to polypeptides as well. Applicant's asserted utility for the polypeptide and polynucleotides is to treat disorders when no nexus has been established between the claimed invention and any specific disease condition. In the instant case, applicant has not even demonstrated that the protein itself is functional within any biological system. The specification does not disclose whether the instantly claimed protein even has a function. Therefore, this is not a specific or substantial utility.

b) The gene is a good target for antagonists which inhibit the biological function of the protein encoded by this gene (pg 39, paragraph 0105). This utility is not specific or substantial. Any protein can be used to screen for agonists or antagonists to itself,

once its function is known. But since applicant has not provided a nexus between polypeptides of SEQ ID NO: 60 or 83 and any disease or condition, a skilled artisan would have no reason to screen for any compound which modulates either the amount or activity of the polypeptides. Additionally, since the function of the polypeptides is not known, considerable further research would be necessary for a skilled artisan to develop an assay to determine whether activity is modulated, i.e. either increased by an agonist or decreased by an antagonist.

Furthermore, since applicant has not demonstrated whether increases or decreases in activity of polypeptides of SEQ ID NO: 60 or 83 are important in disease states, the skilled artisan would not know whether to look for agonists, antagonists, or agents which bind to these polypeptides. Finally, as stated above, since applicant has not provided a nexus between the polypeptides and any disease or condition, considerable further research would be required to know how to use either an agonist or antagonist of polypeptides of SEQ ID NO: 60 or 83, once identified, in the treatment of any disease or condition. Clearly, the asserted utility is not specific or substantial.

c) Polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 11 (pg 38, paragraph 0100). This utility is neither specific nor substantial. Any polynucleotide that comes from an organism can be used in chromosome localization studies, even, for example, sequences that do not encode protein. Therefore the utility is not specific. The revised utility examination guidelines (Federal Register 2001 66(4):1092-1099) indicate that in certain circumstances, isolated nucleic acids *may* be useful in hybridization studies. The far-right column of pg 1094 is

particularly informative: "An isolated and purified DNA molecule may meet the statutory utility requirement if, e.g., it can be used to produce a useful protein or it hybridizes near a disease marker." However, the specification as originally filed does not indicate, or even contemplate, that polynucleotides encoding polypeptides of SEQ ID NO: 60 or 83 hybridize near any disease markers. Therefore, considerable additional research would be required, so this is not a substantial utility.

d) Expression levels of the gene can be used in tissue expression studies to compare healthy and diseased states (pg 38-39). This is not a specific or substantial utility. Any polynucleotide can be used in a tissue expression study, so the asserted utility is not specific. Furthermore, the asserted utility is not substantial. In the absence of knowing any physiological or disease condition associated with expression levels of polypeptides of SEQ ID NO: 60 or 83, determining its expression pattern is basic research. MPEP § 2107.01(I) clearly states that basic research is not a substantial utility.

e) The polypeptides of SEQ ID NO: 60 or 83 can be used to produce antibodies (pg 38). Again, this is not a specific or substantial utility. [Hopp *et al.* (1981. PNAS 78:3824-3828].; see particularly Table 3) teach that any polypeptide fragment of at least 6 amino acids is immunogenic and therefore could be used to make an antibody. But since applicant has not demonstrated a nexus between *SEQ ID NO: 60 or 83* and any disease or condition, there would be no reason to make an antibody against it. Considerable further research would be required to use an antibody. It is acknowledged that antibodies are useful in detecting the antigen against which they are raised.

However, applicant's attention is again directed to MPEP § 2107.01(I), which clearly states that methods of assaying for a product which has no utility do not constitute substantial utilities.According to the text of 35 USC sec. 101, an invention must be "useful". Our reviewing courts have applied the labels, "specific utility" (or "practical utility") to refer to this aspect of the "useful invention" requirement of sec. 101. (Nelson v. Bowler, 626 F.2d 853, 206 USPQ 881, 883 (CCPA 1980)). In Nelson, the court characterized "specific utility" (or "practical utility") as "a shorthand way of attributing real-world value to claimed subject matter". In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." (Id. at 856.)

The claimed proteins are not supported by a specific asserted utility and do not, without further research and experimentation, provide an immediate benefit to the public. Applicant's specification discloses that the claimed proteins are expressed in colon and colon cancer, and the nucleotide sequence of polypeptide SEQ ID NO: 60 have sequence homology with the A33 gene, which is expressed in colon cells (pg 37-40, paragraphs [0099-0105]); however, no specific utility for the claimed proteins are asserted except that they may be useful for diagnosis, treatment and/or detection of proliferative disorders including but not limited to tumors, especially of the intestine, such as, carcinoid tumors, lymphomas, cancer of the colon. Any benefit to the public (to one of ordinary skill in the art) is speculative. There is no basis in the specification upon which to conclude that *any* of the proteins encompassed by the claims are, or will turn out to be, diagnostic or therapeutic after testing. Note, because the claimed invention is

not supported by a specific asserted utility for the reasons just set forth, credibility cannot be assessed.

Claims 25 and 37 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention (see section 9).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a polypeptide at least 95% identical to a mature or full length form of the polypeptide encoded by the HCNDA61 cDNA in ATCC Deposit No. 20381. The specification indicates at page 4 that the deposit was made pursuant to the terms of the Budapest Treaty, lines 4-7. If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, or someone

empowered to make such a statement, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

Claims 25-48 are again rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for polypeptides that comprise an amino acid sequence that shares at least 95% sequence identity with SEQ ID NO: 60 or 83; fragments or variants of SEQ ID NO: 60 or 83; fusion proteins of SEQ ID NO: 60 or 83 with a heterologous polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face,

contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986).

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to the full length polypeptides of SEQ ID NO: 60 or 83, polypeptides which comprise an amino acid sequence that shares at least 95% sequence identity with SEQ ID NO: 60 or 83, fragments of SEQ ID NO: 60 or 83 and fusion proteins of SEQ ID NO: 60 or 83 with a heterologous polypeptide.

The state of the prior art and the predictability or lack thereof in the art: The art teaches that substitution of as little as a single amino acid will alter protein function (Ju,

et al PNAS 88-2658-2662, 1991). For example, Ju *et al* (PNAS 88:2658-2662, 1991) teach that substitution of Lys-145 to Asp will convert the IL-1 receptor antagonist into an agonist. Lederman, *et al* (Mol. Immunol. 28(11):1171-81,1991) teach that a arginine-tryptophan substitution at amino acid 240 of the CD4 molecule abolishes the binding of the monoclonal antibody OKT4. The specification does not describe which part of the polypeptide would convey the function and because the function of a polypeptide correlates with its structure, it would be difficult to predict whether any truncation, substitution or addition would still render the polypeptide functional.

The amount of direction or guidance present and the presence or absence of working examples: The specification does not disclose the functional domains, which are required for functional equivalents and does not disclose the structures that are important for retention of polypeptide activity. The specification fails to provide any guidance as to how to make or use 'fragments' or mutated polypeptides with similar antigenic determinants which retain the function of the full length polypeptide. There are no working examples directed to any truncated polypeptides or fragments which retain the activity of the full length polypeptide.

The breadth of the claims and the quantity of experimentation needed: The claims are directed to a broad spectrum of fragments/variants and polypeptides with at least 95% identity to SEQ ID NOs: 60 or 83. However since the art teaches that there is considerable unpredictability in retaining protein function even with a single amino acid substitution, it would require undue experimentation for a person of skill in the art to be able to use the invention as described.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear what is meant by the phrase ' a first amino acid sequence at least 95% identical to a second amino acid sequence'. What are the limits of the first amino acid compared to the second amino acid? It is unclear whether the first amino acid sequence occur in the N or the C terminal region of the claimed polypeptides and how many amino acid residues comprise the first amino acid sequence.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 25-34 and 37-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Chretien, *et al* (Eur. J. Immunol.28: 4094-4104, 1998).

The claimed invention is drawn to full length polypeptides comprising SEQ ID NOs: 60 or 83, fragments or variants of SEQ ID NOs: 60 or 83, polypeptides with at least 95% identity to SEQ ID NOs: 60 or 83, fusion proteins of SEQ ID NOs: 60 or 83 and glycosylated polypeptides of SEQ ID NOs: 60 or 83.

Chretien, *et al* teach a polypeptide that is 98.4% identical to the claimed polypeptide of SEQ ID NO: 83. Chretien, *et al* teach that CTX, a cortical thymocyte marker in Xenopus is an 'immunoglobulin superfamily (Igsf) member comprising one variable and one constant C2-type Igsf domain, a transmembrane segment and a cytoplasmic tail'(pg 4094). The sequence is shown in Fig 1, pg 4096. The N glycosylation sites are also shown in Figs 1 and 2.

Claims 25-48 are rejected under 35 U.S.C. 102(e) as being anticipated by Lal, *et al* (WO0000610).

The claimed invention is drawn to full length polypeptides comprising SEQ ID NOs: 60 or 83, fragments or variants of SEQ ID NOs: 60 or 83, polypeptides with at least 95% identity to SEQ ID NOs: 60 or 83, fusion proteins of SEQ ID NOs: 60 or 83 and glycosylated polypeptides of SEQ ID NOs: 60 or 83.

Lal, *et al* teach that that human signal peptide-containing protein (HSPP-28) shows 99.7% homology with the polypeptide of SEQ ID NO: 60 from 1-327 aa. Lal, *et al* teach that the protein can be glycosylated, phosphorylated, acetylated, acylated and

carboxylated depending on the host cell strain selected to express the protein (pg 38, lines 26-32, pg 39, lines 1-3). Moreover, Lal, *et al* teach that the recombinant protein can be 'synthesized as a fusion protein with e.g. gluthathione S-transferase (GST) or a peptide epitope tag, such as FLAG or 6-His, thereby permitting rapid, single-step, affinity-based purification of recombinant fusion protein from crude cell lysates (pg 70, lines 12-15).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chretien, *et al* (Eur. J. Immunol.28: 4094-4104, 1998), as applied to claims 25-34 and 37-46 above, in view of Dube, *et al* (J. Biol. Chem. 263: 17516-17521, 1988).

The claimed invention is drawn to full length polypeptides comprising SEQ ID NOs: 60 or 83, fragments or variants of SEQ ID NOs: 60 or 83, polypeptides with at least 95% identity to SEQ ID NOs: 60 or 83, and fusion proteins of SEQ ID NOs: 60 or 83 which are glycosylated.

As set forth *supra*, Chretien, *et al* teach a polypeptide that is 98.4% identical to the polypeptide of instant SEQ ID NO: 83. Chretien does not teach the difference between N or O-glycosylation of the polypeptide.

Dube, *et al* teach that erythropoietin is a glycoprotein that is secreted as a mature protein with three N-linked and one O-linked oligosaccharide chains. Dube, *et al* further teach that prevention of O-linked glycosylation impaired secretion and as O-glycosylation occurs in the Golgi, the oligosaccharide may be important for recognition by secretory mechanisms or for protection of the protein from intravesicular mechanisms (pg 17519, col 2).

Based on the teaching of Chretien, *et al* that the polypeptide of the instant application is an immunoglobulin superfamily (Igsf) member, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the recombinant protein by glycosylation as taught by Dube, *et al.* The person of ordinary skill in the art would have been motivated to glycosylate the protein because absence of glycosylation inhibits secretion.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Betty Lee, Ph.D. whose telephone number is (571) 272-8152. The examiner can normally be reached on M-F 9 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BLL

Brenda Brumback
BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600